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acute side effect (16 pts). There was 1 episode of G3 dyspnea possibly treatment related, but no other >G2 events. One pt developed G2 RT pneumonitis. 9 pts developed late chest pain at 3-21 mo post SBRT; 4 of those developed rib fractures in the RT field area, 11-21 mo post SBRT. In 38 evaluable pts (40 tumors), 6 CR and 24 PR were observed. There were no local failures in 36 pts with peripheral tumors, but 2 failures in pts treated with the lower 50 Gy/10 fr schedule. CBCT tumor matching compared to bone matching resulted in a mean difference of 6.8mm (±4.9), the difference was >13.9 mm in 10% of pts; this would have resulted in very significant tumor miss if portal imaging was used without proper visualization of the target.

Conclusion: These results confirm that lung SBRT gives high rates (95%) of local control with the only local failures observed in the centrally-located tumors treated with lower dose of 50 Gy/10 fr. Acute toxicity is low; rib fracture is the most common late toxicity. CBCT greatly improves the accurate delivery of high radioablative doses of SBRT for early stage lung cancer.

PD5-2-4 Clinical Data from Radiation Therapy, Thu, 12:30 - 14:15

Phase I/II results of RTOG L-0117; a phase I/II dose intensification study using 3DCRT and concurrent chemotherapy for patients with inoperable NSCLC

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Background: The standard radiation dose for NSCLC was established by RTOG 7301 as 60 Gy. Local failure rates with this dose remain unacceptably high. In preparation for a anticipated Phase III comparison of high dose versus standard dose radiation therapy, this Phase I/II study was initiated to establish the maximum tolerated dose (MTD) of radiation therapy, in the setting of concurrent chemotherapy, using 3DCRT for NSCLC.

Methods: Eligibility included patients with histologically proven, unresectable Stages I-III NSCLC and a Zubrod perfomance status of 0-1. Weight loss eligibility was <10%. Concurrent chemotherapy consisted of paclitaxel 50 mg/m^2 and carboplatin AUC=2 given weekly. Radiation (RT) dose was started at 75.25 Gy/35 fractions. Once the MTD was reached, the phase II portion of the study was initiated and continues to accrue. Radiation therapy volumes consisted of gross tumor and nodes plus a margin. Elective lymph nodes were not included in the treatment fields. Technical criteria included strict dosimetric constraints on the normal lung (V20 <30%) and esophagus (mean dose <34 Gy and V55 < 30%) and water-based dose calculations prescribed to the isocenter.

Results: The Phase I portion of this study accrued 17 patients from 8 institutions and was closed in January 2004. After the initial 8 patients were accrued to Arm 1, the trial closed temporarily on September 26, 2002 due to reported toxicity. Two acute treatment-related DLTs were reported: a grade 5 infection/febrile neutropenia and a grade 3 pneumonitis. The protocol, therefore, was revised to de-escalate the RT dose (74 Gy/37 fractions). Arm 2 accrued 9 patients with 2 (22%) developing Grade 3 GI toxicities and 1 (11%) reporting a Grade 3 infection/febrile neutropenia. Phase II has accrued 31 eligible patients at 74 Gy. Of the 27 (87%) patients with acute toxicity information, there were 3 (11%) Grade 3 pain toxicities, 2 (7%) Grade 3 infection/febrile neutropenia toxicities, 1 (4%) Grade 3 pulmonary toxicity, and 1 (4%) Grade 3 skin toxicity. A total of 13 (48%) patients reported grade 3+ non-hematologic toxicities.

Conclusions: The MTD was determined to be 74 Gy/37 fractions (2.0 Gy per fraction) using 3DCRT with concurrent paclitaxel and carboplatin. Four (11%) grade 3 pulmonary or infection/febrile neutropenia toxicities have occurred at the 74 Gy dose level. The Phase II component of RTOG L-0117 will close with the opening of our Phase III trial (RTOG 0617).

PD5-2-5 Clinical Data from Radiation Therapy, Thu, 12:30 - 14:15

Local therapy of primary diseae improves survival in non-small cell lung cancer metastatic to a single organ - a lesson from brain metastases

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Introduction: The standard therapy for non-small cell lung cancer (NSCLC) brain metastases involves radiotherapy and/or surgical resection for all visible lesions. This practice has been based on the assumption that brain metastases are less sensitive to systemic therapies and has been shown to palliate brain metastasis-related symptoms and to improve survival. Similarly, we hypothesize that additional local therapy for other sites of disease, particularly the primary tumor and locoregional lymph node metastases, may further improve survival.

Methods: Patients with metastatic NSCLC who received ablative local therapy of primary disease - radiotherapy (≥ 45 Gy) or surgical resection of their primary tumor and locoregional lymph nodes - tend to have a low volume of disease prior to treatment. To identify those who received this definitive local therapy, we searched the M.D. Anderson Cancer Center Tumor Registry, Thoracic Radiation Oncology, and Neurosurgery databases, for patients with only one organ site of metastasis and analyzed their overall survival based on definitive local therapy of primary disease and the presence or absence of brain metastases.

Results: 120 patients had brain as a solitary organ site of metastases; of them 115 (96%) received local therapy for brain metastases - surgical resection, stereotactic radiosurgery, and/or whole brain radiotherapy. Of these 120, 10 (8%) also received ablative local therapy of primary disease - 8 (6%) with radiotherapy ≥ 45 Gy or 2 (2%)with surgical resection of primary tumor and locoregional lymph nodes. Another 221 patients had a solitary organ site of metastasis outside the brain; of them 61 (28%) received local palliative radiotherapy for metastases. Of these 221, 35 (16%) also received ablative local therapy of primary disease - 33 (15%) with radiotherapy ≥ 45 Gy or 2 (1%) with surgical resection of primary tumor and locoregional lymph nodes. In those with brain as a solitary organ site of metastasis and single metastasis, there was a marked improvement in survival with resection or radiotherapy ≥ 45 Gy for primary thoracic disease (p=0.00186, median survival 30 vs. 7 months). In those with non-CNS solitary organ sites of metastases, there is only a tendancy towards improved survival in

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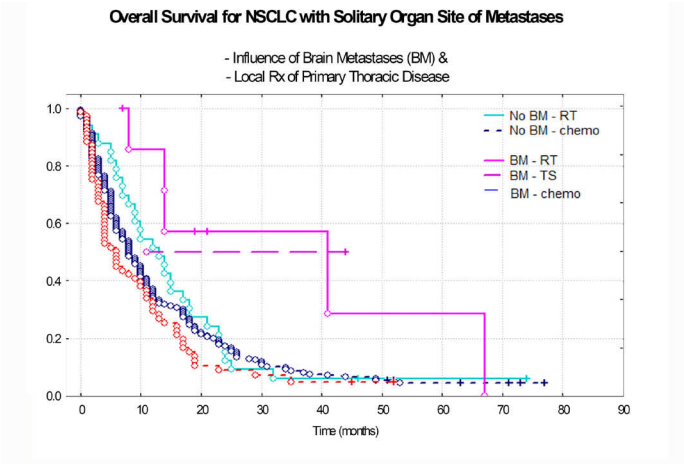
patients who receive similar local therapy of primary disease (median survival 12 vs. 8 months).



Conclusions: For NSCLC patients with brain as a solitary organ site of metastasis and a single brain metastasis, radiotherapy or resection for primary lung disease markedly improves median survival. For those with extracranial solitary organ sites of metastases, local therapy of primary thoracic disease improves survival, but this benefit is lost in those who survive beyond one year. Patients with extracranial metastases rarely received local therapy for metastases, whereas brain metastasis patients invariably do. Our results suggest a potential benefit and need for a prospective study of surgical resection or radiotherapy to all visible disease in patients with oligometastatic NSCLC.

PD5-2-6 **Clinical Data from Radiation Therapy, Thu, 12:30 - 14:15**

Hypofractionated stereotactic body radiotherapy in patients with peripherally or centrally located medically inoperable stage I or isolated recurrent non-small cell lung cancer

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Background: To evaluate the therapeutic efficacy and treatment-related toxicity of image-guided hypofractionated stereotactic body radiotherapy (SBRT) in patients with peripherally or centrally located, medically inoperable stage I or isolated recurrent NSCLC.

Methods: Subjects had pathologically confirmed stage I (n=49) or isolated recurrent (n=24) NSCLC. Among 73 patients, 25 patients had centrally located lesions defined as within 2 cm of bronchial tree, major vessels, esophagus, heart and other mediastinal structures but no direct invasion. Internal gross target volume was delineated using maximal intensity projection created by combining the data from a 4-D CT dataset at different respiratory phases. The clinical target volume was the internal gross target volume plus an 8-mm margin, and a 3-mm setup uncertainty margin was added to determine the planning target volume. For each fraction the patient was aligned using in-room CT-on-rails. The prescribed dose was 50 Gy to PTV at daily 12.5 Gy/fraction for 4 contiguous days. Dose constraint of major mediastinal critical organs was 40 Gy less than 10 cc except for esophagus in which 40 Gy was limited to less than 1 cc.

Results: Median follow-up was 18 months (3-28 months). The overall progression-free survival rate at the treated site was 95.9%. For stage I disease, the complete response (CR), partial response (PR) and stable disease (SD) rate were 33%, 35% and 31% respectively. There was no significant difference in response rate between stage Ia (n=42) and Ib (n=7). Two patients (4.1%) developed mediastinal lymph node metastasis. For isolated recurrent disease, the CR, PR and SD rate were 45.8%, 33.3%, and 12.5% respectively. Mediastinal lymph node metastasis happened in three patients (12.5%). There was 6.1% grade II but no grade III and above radiation pneumonitis in stage I disease. Three patients with recurrent disease had worse dyspnea after SBRT and one patients needed nasonal oxygenation. No esophagitis was noted. 22.8% of patients developed grade II dermatitis at the treated site that appears related to the dose (>35 Gy) and volume of the skin treated. Three patient developed chronic skin scar and five patients had chronic mild neurogenic chest pain due to intercostal nerve injury. There was no increased toxicity noted in centrally located lesions compared with peripherally located lesions.

Conclusions: Image-guided SBRT using 50 Gy in four fractions achieved excellent local progression-free survival rate with minimal toxicity in peripherally or centrally located stage I or isolated recurrent NSCLC. Long-term follow up and further studies are needed to evaluate the toxicity of centrally located lesions and higher dose volume constraints to critical structures.

PD5-2-7 **Clinical Data from Radiation Therapy, Thu, 12:30 - 14:15**

Hiperfractionated (HFRT) versus Standard Radiotherapy (SRT) in Locally Advanced (LA) NSCLC: a metaanalysis of randomized phase III trials

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Background: Radiotherapy is the cornerstone treatment for unresectable LA-NSCLC. Outcomes with standard RT scheduling in this patient subgroup are poor and new approaches like altered fractionation were studied. Even though many trials investigated the value of these new strategies, their results were inconsistent. We performed a meta-analysis of those trials to try to clarify this matter.

Methods: We performed a thorough literature search to identify phase III randomized trials where standard RT was compared with an altered RT fractionation in the treatment of LA-NSCLC. The trials were analysed for any relevant end point and a meta-analysis of the selected trials was performed.

Results: We found 6 trials with n=1484 (n=793 for HFRT and n=691 for SRT). An absolute improvement in mortality rate of 4.2% with HFRT was shown: 90.7% for SRT vs 86.5% for HFRT ($p<0.02$), with a HR=0.65 (CI 95%: 0.47-0.90). Results persist even excluding RTOG 8808 and CHART. Two year survival was also improved (31.8 vs 26.1%). Response rate (data available from 2 studies) were similar: 60.8 vs. 52.5%; HFRT was associated with a reduction of 28% in local failures (HR: 0.72, CI: 0.56-0.93). Toxicity: HFRT produced a significantly increased incidence of Grade 3 and 4 esophagitis (18.1 vs. 8.7%, $p<0.001$); but grade 3/4 pneumonitis was less frequent with HFRT (8.2 vs. 11.6%, $p<0.02$).

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